Amendments to the Specification:

Please amend the specification as follows:

Please replace paragraph starting at page 4, line 22, with the following rewritten paragraph:

Figures ~~1A, 1B and 1C~~ Figures 1A – 1G. Human MCK-10 nucleotide sequence and deduced amino acid sequence. Regions of interest include the signal sequence (amino acids (aa) 1-18); the Discoidin I-like doman (aa 31-185); the putative precursor cleavage sit (aa 304-307); the transmembrane region (aa 417-439); the alternatively spliced sequence I (aa) 505-541); the alternatively spliced sequence II (aa 666-671); and the peptide antibody recognition sequences: NTα:aa 25-42, NTβ:aa 309-321, CTβ:aa 902-919.

Please replace paragraph starting at page 4, line 33, with the following rewritten paragraph:

Figures ~~3A, 3B, 3C and 3D~~ 3A – 3H. Human CCK-2 nucleotide sequence and deduced amino acid sequence.

Please replace paragraph starting at page 5, line 1, with the following rewritten paragraph:

~~Figure 4A~~ Figures 4A and 4B. Shared sequence homology between MCK-10 and CCK-2.

Please replace paragraph starting at page 5, line 3, with the following rewritten paragraph:

Figure ~~4B~~ 4C. Shared regions of homology between MCK-10 and CCK-2.

Please replace paragraph starting at page 8, line 18, with the following rewritten paragraph:

For clarity of discussion, the invention is described in the subsections below by way of example for the MCK-10 gene depicted in Figures ~~1A, 1B and 1C~~ 1A – 1G and the CCK-2 gene depicted in Figures ~~3A, 3B, 3C and 3D~~ 3A – 3H. However, the principles may be analogously applied to differentially spliced isoforms of MCK-10 and to other members of the MCK-10 family of receptors.

Please replace paragraph starting at page 8, line 28, with the following rewritten paragraph:

The nucleotide coding sequence and deduced amino acid sequence of the human MCK-10 gene is depicted in Figures ~~1A, 1B and 1C~~ 1A – 1G (SEQ. ID NO. 1). In accordance with the invention, any nucleotide sequence which encodes the amino acid sequence of the MCK-10 gene product can be used to generate recombinant molecules which direct the expression of MCK-10. In additional embodiments of the invention, nucleotide sequences which selectively hybridize to the MCK-10 nucleotide sequence shown in FIG. ~~1A, 1B and 1C~~ 1A – 1G (SEQ ID NO: 1) may also be used to express gene products with MCK-10 activity. Hereinafter all such variants of the MCK-10 nucleotide sequence will be referred to as the CK-10 DNA sequence.

Please replace paragraph starting at page 9, line 6, with the following rewritten paragraph:

In a specific embodiment described herein, the human MCK-10 gene was isolated by performing a polymerase chain reaction (PCR) in combination with two degenerate oligonucleotide primer pools that were designed on the basis of highly conserved sequences within the kinase domain of receptor tyrosine kinases corresponding to the amino acid sequence HRDLAA (sense primer) and SDVWS/FY (antisense primer) (Hanks et al., 1988). As a template cDNA synthesized by reverse transcription of poly-A RNA from the human mammary carcinoma cell line MCF7, was used. A novel RTK, designated MCK-10 (mammary carcinoma kinase 10) was identified that within the tyrosine kinase domain exhibited extensive sequence similarity to the insulin receptor family. The PCR fragment was used to screen a lambda gt11 library of human fetal brain cDNA (Clontech). Several overlapping clones were identified. The composite of these cDNA clonase is depicted in Figures ~~1A, 1B and 1C~~ 1A – 1G. Furthermore, screening of a human placental library yielded two cDNA clonse, MCK-10-1 and MCK-10-2, which encoded the entire MCK-10 protein but contained a shorter 5' untranslated region starting at position 278 of the MCK-10 sequence (Figures ~~1A, 1B and 1C~~ 1A – 1G). Sequences analysis of the two clones revealed complete identity with the exception of 111 additional nucleotides within the juxtamembrane domain, between nucleotides 1832 and 1943. One of the clones isolated from the human fetal brain library contained an additional 18 nucleotides in the tyrosine kinase domain. These sequences were in-frame with the MCK-10 open reading frame and did not contain any stop codons. The MCK-10 splice isoforms have been designated MCK-10-1 (with the additional 111 bp), MCK-10-2 (without any insertions), MCK-10-3 (with the additional 111 bp and 19 bp), and MCK-10-4 (with the additional 18 bp) (FIG. 2).

Please replace paragraph starting at page 10, line 7, with the following rewritten paragraph:

As shown in Figures ~~1A, 1B, and 1C~~ 1A – 1G and Figures ~~3A, 3B, 3C and 3D~~ 3A – 3H, MCK-10 have all of the characteristics of a receptor PTK: the initiation codon is followed by a stretch of essentially hydrophobic amino acids, which may serve as a signal peptide. Amino acids 417-439 are also hydrophobic in nature, with the characteristics of a transmembrane region. The extracellular domain encompasses 4 consensus N-glycosylation sites (AsnXSer/Thr) and 7 cysteine residues. The extracellular region is shorter than that of the insulin receptor family and shows no homology to other receptor tyrosine kinases, but contains near the N-terminus the consensus sequences for the discoidin I like family (Poole et al. 1981, J. Mol. Biol. 153:273-289), which are located as tandem repeats in MGP and BA46, two milk fat globule membrane proteins (Stubbs et al. 1990, Proc. Natl. acad. Sci. USA, 87, 8417-8421, Larocca et al. 1991, Cancer Res. 51: 4994-4998), in the light chains of factor V (Kane et al. 1986, proc. Natl. Acad. Sci. USA, 83: 6800-6804) and VIII (Toole et al. 1984, Nature 312: 342-347), and in the A5 protein (Takagi et al. 1987, Dev. Biol., 122: 90-100).

Please replace paragraph starting at page 15, line 17, with the following rewritten paragraph:

The present invention also relates to other members of the MCK-10 family of receptor kinases. Members of the MCK-10 family are defined herein as those DNA sequences capable of hybridizing to MCK-10 DNA sequences as presented in Figures ~~1A, 1B and 1C~~ 1A – 1G. Such receptors may demonstrate 80% homology at the amino acid level in substantial stretches of DNA sequences. In addition, such receptors can be defined as those receptors containing an intracellular tyrosine kinase domain and a discoidin I sequence located near the amino-terminal end of the protein. The discoidin I domain is defined as that region of MCK-10 located between amino acid 31-185 as presented in Figure 1.

Please replace paragraph starting at page 15, line 31, with the following rewritten paragraph:

In a specific embodiment of the invention described herein, an additional member of the MCK-10 family of receptor tyrosine kinases was cloned and characterized. The nucleotide coding sequence and deduced amino acid sequence of the novel receptor tyrosine kinase, herein referred to as CCK-2, is presented in Figures ~~3A, 3B, 3C and 3D~~ 3A – 3H. In accordance with the invention, any nucleotide sequence which encodes the amino acid sequence of the CCK-2 gene product can be used to generate recombinant molecules which direct the expression of CCK-2. In additional, embodiments of the invention, nucleotide sequences which selectively hybridize to the CCK-2 nucleotide sequence as shown in Figures ~~3A, 3B, 3C and 3D~~ 3A – 3H (SEQ. ID NO: 2) may also be used to express gene products with CCK-2 activity.

Please replace paragraph starting at page 16, line 11, with the following rewritten paragraph:

Analysis of the CCK-2 sequence revealed significant homology to the extracellular, transmembrane and intracellular region of the MCK-10 receptor indicating that it was a member of the MCK-10 family of receptors. The shared homology between CCK-2 and MCK-10 is depicted in ~~Figure 4A and 4B~~ Figures 4A – 4C.

Please replace paragraph starting at page 38, line 33, with the following rewritten paragraph:

The partial cDNA sequence of the new MCK-10 RTK, which was identified by PCR, was used to screen a λgt11 library from human fetal brain cDNA (Clontech) (complexity of $1x10^{10}$ recombinant phages). One million independent phage clones were plated and transferred to nitrocellulose filters following standard procedures (Sambrook, H.J., Molecular Cloning, Cold Spring Harbor Laboratory Press, USA, 1989). The filters were hybridized to the EcoRI/EcoRI fragment of clone MCK-10, which had been radioactively labeled using 50μCi [α^{32}P]ATP and the random-primed DNA labeling kit (Boehringer Mannheim). The longest cDNA insert (8) of ~3500 bp was digested with the restriction enzymes EcoRI/SacI to

obtain 5' end probe of 250 bp. This probe was used to rescreen the human fetal brain library and several overlapping clones were isolated. The composite of the cDNA clones are shown in Figures ~~1A, 1B and 1C~~ 1A – 1G. Some of the clones had a deletion of 6 amino acids at position 2315 in the MCK-10 sequence.

Please replace paragraph starting at page 39, line 17, with the following rewritten paragraph:

The 1.75 million independent phage clones of a human placenta library, λZAP were plated and screened with the 5' end probe (EcoRI/SacI) of clone 8. Two clones were full-length with a shorter 5' end starting at position 278 of the nucleotide sequence shown in Figures ~~1A, 1B and 1C~~ 1A – 1G. Subloning of positive bacteriophages clones into pBluescript vector was done by the *in vivo* excision protocol (Stratagene).

Please replace paragraph starting at page 42, line 20, with the following rewritten paragraph:

To identify novel receptor tyrosine kinases (RTKs) that are expressed in mammary carcinoma cell lines, we used the polymerase chain reaction in combination with two degerate oligonucleotide primer pools based on highly conserved sequences within the kinase domain of RTKs, corresponding to the amino acid sequence HRDLAA (sense primer) and SDVWS/FY (antisense primer) (Hanks et al. 1988, Science 241, 42-52), in conjunction with cDNA synthesized by reverse transcription of poly A RNA from the human mammary carcinoma cell line MCF7. We identified a novel RTK, designated MCK-10 (mammary carcinoma kinase 10), that within the tyrosine kinase domain exhibited jextensive sequence similarity to the insulin receptor family. The PCR fragment was used to screen a lambda gt11 library of human fetal brain cDNA (Clontech). Several overlapping clones were identified and their composite sequence is shown in Figures ~~1A, 1B and 1C~~ 1A – 1G. Furthermore, screening of a human placenta library yielded two cDNA clones which encoded the entire MCK-10 protein but whose 5' nucleotide sequence began at nucleotide 278 in the sequence shown in Figure 1. Sequence analysis of the two clones revealed complete identity with the exception of 111 additional nucleotides within the juxtamembrane domain, between

nucleotides 1832 and 1943. One of the clones isolated from the human fetal brain library contained an additional 18 nucleotides in the tyrosine kinase domain. These sequences were in-frame with the MCK-10 open reading frame and did not contain any stop codons. We designated these MCK-10 splice isoforms MCK-10-1 (with the additional 111 bp, MCK-10-2 (without any insertions), MCK-10-3 (with the additional 111 bp and 18 bp), and MCK-10-4 (with the additional 18 bp). This new receptor tyrosine kinase was recently described by Johnson et al. (1993, Proc. Natl. Acad. Sci. USA, 90 5677-5681) as DDR.

Please replace paragraph starting at page 47, line 25, with the following rewritten paragraph:

The precursor and the β-subunit of MCK-10 showed strong tyrosine phosphorylation after orthovanadate treatment, (~~FIG. 4A~~ FIGS. 4A and 4B, left panel). Surprisingly, the MCK-10-1, containing the 37 amino acid insertion, exhibited lower kinase activity than MCK-10-2. Reprobing the same blot with a peptide antibody raised against the MCK-10 C-terminus revealed equal amounts of expressed receptor and a slight shift of MCK-10-1 precursor and β-subunit due to the additional 37 amino acids of the insertion (~~FIG. 4A~~ FIGS. 4A and 4B, right panel).

Please replace paragraph starting at page 48, line 1, with the following rewritten paragraph:

We further analyzed the N-linked glycosylation of the splice variants. Transfected cells were treated overnight with tunicamycin, which inhibits the maturation of proteins by glycosylation. Two affinity purified antibodies raised against peptide sequence of MCK-10 N- and C-terminus, respectively, were used for subsequent immunoprecipitations. Both antibodies precipitated the predicted 101 kD or 97 kD polypeptides from tunicamycin-treated cells (FIG. ~~4B~~ 4C). Interestingly, the size of the fully glycosylated forms of MCK-10-1 and MCK-10-2 suggested that the latter was more extensively glycosylated than the putative alternative splice form. This data indicates that the 37 amino acid insertion of MCK-10-1 influences its posttranslational modification which may influence ligand.

Please replace paragraph starting at page 50, line 3, with the following rewritten paragraph:

An additional member of the MCK-10 receptor tyrosine kinase family was identified using a polymerase chain reaction and cDNA prepared from colonic adenocarcinoma RNA. The nucleotide sequence of the novel receptor, designated CCK-2, is presented in Figures 3A and 3B. Analysis of the CCK-2, nucleotide sequence and encoded amino acid sequence indicated significant homology with MCK-10 throughout the extracellular, transmembrane and intracellular region of the MCK-10 receptor. The regions of homology between CCK-2 and MCK-10 extend into the N-terminus consensus sequence for the discoidin I like family of proteins. (Poole et al. 1981, J. Mol. Biol. 153, 273-289). The homology between CCK-2 and MCK-10 is diagramed in ~~Figure 4A and 4B~~ Figures 4A – 4C.

Drawings:

Please substitute the attached 39 sheets (Fig. 1A – Fig. 21B) of formal drawings for the informal drawings originally filed with the application. A separate Transmittal of Formal Drawings is submitted.

The drawing sheets attached in connection with the above-identified application containing Figures 1A – 21B are being presented as new formal drawing sheets to be substituted for the previously submitted drawing sheets. No new matter has been added to the figures.